

***Remarks***

Reconsideration of this Application is respectfully requested.

The foregoing amendments to the claims are believed to place the claims into condition for immediate allowance or into better condition for consideration on appeal. It is respectfully believed that these amendments do not raise new issues that would require an additional search.

No new matter is added to the present application by the foregoing amendments, which are fully supported in the specification as originally filed. Accordingly, their entry is respectfully requested. Upon entry of the foregoing amendment, claims 1, 8, 10-12 and 42 are pending in the application, with claims 1 and 42 being the independent claims. Support for the amendments in claims 1 and 42 can be found on page 21 of the specification.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejections under 35 U.S.C. § 112, first paragraph***

In the Office Action, at page 2, the Examiner rejected claims 1, 2, 8-12 and 42 under 35 U.S.C. § 112, first paragraph for allegedly not being enabled for variants or fragments of SEQ ID NO:1. Applicants have previously cancelled claim 9, thus rendering its rejection moot. Applicants respectfully traverse the rejection as it may apply to the remaining claims. Solely in an effort to expedite prosecution, and without acquiescing with the propriety of the rejection, Applicants have cancelled claim 2, thus rendering the rejection of claim 2 moot.

In the Office Action, at page 3, the Examiner alleges that Applicants have only taught the amino acid sequence of SEQ ID NO:1. The Examiner further alleges that Applicants have provided "little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change. . . ." The Examiner cites the data in Voet to support his argument that even a single amino acid change can cause drastic and unpredictable effects on protein structure and function. Applicants have tested many muteins and mapped the positions that tolerate substitution. Applicants respectfully draw the Examiner's attention to pages 64-71 in which experiments testing the activity of muteins with single and multiple amino acid substitutions are described. The data from these tests provides ample guidance for a person skilled in the art as to which positions are tolerant of substitution. Moreover, the tests to measure the function of the claimed muteins are also described in detail in the specification. Thus, the Examiner is incorrect in stating that "detailed information regarding the structural and functional requirements of the encoded proteins are lacking." Office action at 4.

In the Office Action, at page 4, the Examiner alleges that Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of SEQ ID NO:1. Moreover, the Examiner alleges that the specification does not provide guidance or direction regarding which structural features are required in order to provide activity. Applicants disagree and respectfully point out that they have drawn the Examiner's attention to multiple examples of muteins and fragments of a polypeptide having the sequence of SEQ ID NO:1 in the Reply to the Office Action filed on September 17, 2003. For example, the Examiner is urged to review Example 2, Table 2; Example 6, Table 3; Example 7, Table 4; and Figures 1-7, in which the biological activity of several muteins and

fragments of a polypeptide having the sequence of SEQ ID NO:1 is measured in different experimental systems. Furthermore, as discussed above, Applicants have provided ample guidance as to the structural features that enable a mutein or variant to maintain activity by elucidating the substitution-tolerant positions in the peptide (*see, e.g.*, pages 64-71).

Applicants note that they are not required to provide experimental examples of each and every functional derivative that would fall under the scope of the claims. *See, e.g., Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1237, quoting *In re Angstadt*, 537 F.2d 498, 502, 190 U.S.P.Q. (BNA) 214, 218 (CCPA 1976) ("it is not necessary that a patent applicant test all the embodiments of his invention. . . . what is necessary is that he provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims."). Applicants disagree and reiterate that the specification provides ample guidance as to the position and nature of the substitutions that would enable a peptide to maintain biological activity. However, solely in an effort to expedite prosecution, and without acquiescing with the propriety of the rejection, Applicants have cancelled claim 2 and amended claim 1 to make explicit that which was implicit by adding the phrase "substantially similar to the biological activity of parathyroid hormone" to describe the biological activity of the claimed peptides.

In the Office Action, at page 5, the Examiner alleges that "the term 'biological activity' is not clear as set forth in the rejection under 35 USC 112 second paragraph, *infra*. Thus the skilled artisan would not be apprised of the metes and bounds of the functional limitation with regard to SEQ ID NO: 1 activity." Applicants reiterate the arguments stated in the Reply to the Office Action filed on September 17, 2003. However, solely in an effort to expedite prosecution, and without acquiescing with the propriety of this aspect of the rejection, Applicants have amended the claims to make explicit that which was implicit by

adding the phrase "substantially similar to the biological activity of parathyroid hormone" to describe the biological activity of the claimed peptides. Therefore, Applicants believe that they have addressed the Examiner's concern, stated at page 5.

In the Office Action, at page 5, the Examiner further alleges that it would require undue experimentation for one of skill in the art to make and use the claimed polypeptides, since the skilled artisan would have to first make polypeptide variants of SEQ ID NO:1, then determine a function, then test for that function. The Examiner further alleges that Applicants have not taught how to make polypeptide variants of SEQ ID NO:1. Applicants respectfully disagree: as discussed above, the specification provides ample guidance as to both the tolerable substitutions and the function of the peptides claimed in the present application. Therefore, undue experimentation would not be required to practice the invention.

In the Office Action, at page 6, the Examiner rejected claim 12 for allegedly encompassing subject matter that "would require undue experimentation for one of skill in the art to make and use the claimed variant polypeptides as a pharmaceutical composition since the claims as written do not set forth a function that the claimed polypeptides must possess..." Applicants believe that by adding the phrase "substantially similar to the biological activity of parathyroid hormone" to describe the biological activity of the claimed peptides to claim 1, from which claim 12 depends, Applicants have addressed the Examiner's concern, stated at page 6, regarding claim 12, which is directed to a pharmaceutical composition comprising a polypeptide of the invention. Therefore, the rejection is now moot.

In the Office Action on page 7, the Examiner also rejected claims 2, 8-12 and 42 under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventors had possession of the claimed invention at the time that the application was filed. Applicants respectfully traverse this rejection. Solely in an effort to expedite prosecution, and without acquiescing in the propriety of the rejection, however, Applicants have previously cancelled claim 9, and have currently cancelled claim 2, thus rendering their rejection moot. Applicants reiterate the arguments stated in the Reply to the Office Action filed on September 17, 2003 at pages 15-17. Specifically, Applicants respectfully disagree with the Examiner's statement that no common structural attributes identify the members of the genus: all the claimed peptides have at least nine out of fourteen amino acids in common, *i.e.*, a common primary structure of the molecule. Moreover, the peptides of the genus all have the same functional characteristics, which are amply described in the specification and are now implicitly stated in the claims, *i.e.*, a biological activity substantially similar to the biological activity of parathyroid hormone. Hence, Applicants respectfully assert that the specification provides sufficient written description to convey to one of ordinary skill in the art that Applicants had possession of the full scope of the claimed invention upon filing of the application.

Applicants wish to remind the Examiner that "[a]dequate description under the first paragraph of 35 U.S.C. 112 does not require *literal* support for the claimed invention . . . . the observation of a lack of literal support does not, in and of itself, establish a *prima facie* case for lack of adequate descriptive support under the first paragraph of 35 U.S.C. 112." *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. Int. 1994). Instead, the written description requirement of 35 U.S.C. § 112, first paragraph, is met "if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an [applicant] had possession of the concept of what is claimed," *id.* *I.e.*, "[i]f a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time

of filing, even if every nuance of the claims is not explicitly described in the specification . . . .” *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996). As discussed above, Applicants provide the results of experiments testing over 100 different peptides in the specification. Applicants respectfully assert that the summarized results constitute a sufficient description of a representative number of species by actual reduction to practice to satisfy the written description requirement.

In view of the foregoing amendments and explanations, Applicants respectfully request that the rejection of claims 1, 8, 10-12 and 42 under 35 U.S.C. § 112, first paragraph, be withdrawn.

***Rejections under 35 U.S.C. § 112, second paragraph***

In the Office Action, at page 9, the Examiner rejected claims 1-2, 8, 10-12 and 42 under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter of the invention. The Examiner alleges that “[c]laims 1-2, 8, 10-12, 42 are vague and indefinite in the recitation of the term ‘biologically active’. The term ‘biologically active’ is not defined by the claim, and give no definition of what this activity is.” By the foregoing amendments, Applicants have cancelled claim 2, thus rendering its rejection moot. Applicants respectfully traverse the rejection as it may apply to the remaining claims and reiterate the arguments stated in the Reply to the Office Action filed on September 17, 2003. However, solely in an effort to expedite prosecution, and without acquiescing in the propriety of the rejection, Applicants have amended the other rejected claims to make explicit that which was implicit in the claims by adding the phrase “substantially similar to the biological activity of parathyroid hormone” to describe the biological activity of the claimed peptides. Therefore, Applicants believe that they have

addressed the Examiner's concern, stated at page 9, regarding the definition of biological activities.


### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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